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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/899,381	07/02/2001	Glenda C. Delenstarr	10010760-1	3033

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Agilent Technologies, Inc.
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EXAMINER	
SISSON, BRADLEY L	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 05/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/899,381	DELENSTARR ET AL.	
	Examiner	Art Unit	
	Bradley L. Sisson	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13 and 15-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13 and 15-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 July 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Supplemental Office Action

1. The following is a supplemental Office action. The period of response is reset from the date of mailing of this Office action.

Continued Examination Under 37 CFR 1.114

2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 23 February 2004 has been entered.

Specification

3. The specification is objected to as documents have been improperly incorporated by reference. In particular, the specification states at paragraph 36, found at page 8: "All patents, patent publications, and publications mentioned herein, whether *supra* or *infra*, are hereby incorporated by reference in their entirety." Such omnibus language fails to specify what specific information applicant seeks to incorporate by reference and similarly fails to teach with detailed particularity just where that specific information is to be found in each of the cited documents. As set forth in *Advanced Display Systems Inc. v. Kent State University* (Fed. Cir. 2000) 54 USPQ2d at 1679:

> Incorporation by reference provides a method for integrating material from various documents into a host document--a patent or printed publication in an anticipation determination--by citing such material in a manner that makes it clear that the material is effectively part of the host document as if it were explicitly contained therein. *See General Elec. Co. v. Brenner*, 407 F.2d 1258, 1261-62, 159 USQP 335, 337 (D.C. Cir. 1968); *In re Lund*, 376 F.2d 982, 989, 153 USPQ 625, 631 (CCPA 1967). **To incorporate material by reference, the host document must identify with detailed particularity what specific material it incorporates and clearly indicate where that material is found in the various documents.** *See In re Seversky*, 474 F.2d 671, 674, 177 USPQ 144, 146 (CCPA 1973) (providing that incorporation by reference requires a statement "clearly identifying the subject matter which is incorporated and where it is to be found"); *In re Saunders*, 444 F.2d 599, 602-02, 170 USPQ 213, 216-17 (CPA 1971) (reasoning that a rejection or anticipation is appropriate only if one reference "expressly incorporates a particular part" of another reference); *National Latex Prods. Co. v. Sun Rubber Co.*, 274 F.2d 224, 230, 123 USPQ 279, 283 (6th Cir. 1959) (requiring a specific reference to material in an earlier application in order to have that material considered a part of a later application); *cf. Lund*, 376 F.2d at 989, 13 USPQ at 631 (holding that **a one sentence reference to an abandoned application is not sufficient to incorporate from the abandoned application into a new application**). (Emphasis added.)

Accordingly, the cited documents are not considered to have been properly incorporated by reference and as such, have not been considered with any effect towards their fulfilling, either in part or in whole, the enablement, written description, or best mode requirements of 35 USC 112, first paragraph.

Claim Objections

4. Claims 15 and 16 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. In the present case, claims 15 and 16 both depend from canceled claim 14.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 13 and 15-23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Attention is directed to the decision in *University of Rochester v. G.D. Searle & Co.* 68 USPQ2D 1424 (Fed. Cir. 2004) at 1428:

> To satisfy the written-description requirement, the specification must describe every element of the claimed invention in sufficient detail so that one of ordinary skill in the art would recognize that the inventor possessed the claimed invention at the time of filing. Vas-Cath, 935 F.3d at 1563; see also Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572 [41 USPQ2d 1961] (Fed. Cir. 1997) (patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention"); In re Gosteli, 872 F.2d 1008, 1012 [10 USPQ2d 1614] (Fed. Cir. 1989) ("the description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed"). Thus, an applicant complies with the written-description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572.

7. For convenience, claim 13, the only independent claim, is reproduced below.

13. (Currently Amended) A method of detecting the presence of an analyte nucleic acid in a sample, said method comprising:

(a) providing a nucleic acid array comprising:

(i) at least one hybridization feature to which said analyte nucleic acid specifically binds under stringent hybridization conditions; and

(ii) at least one background feature;

(b) contacting said nucleic acid array with said sample under stringent hybridization conditions;

(c) washing said nucleic acid array;

(d)~~(c)~~ detecting a hybridization signal from said hybridization feature and background signal from said background feature;

(e)~~(d)~~ subtracting said background signal from said hybridization signal to obtain a background corrected hybridization signal; and

(f)~~(e)~~ relating said background corrected hybridization signal to the presence of said analyte target nucleic acid in said sample to detect the presence of said analyte target nucleic acid in said sample;

wherein said method is further characterized by including a target nucleic acid labeling step prior to said detecting step (d).

For purposes of examination, the claimed method has been interpreted as requiring at least one "hybridization feature" which further comprises at least one "background feature." Attention is directed to page 15 of the specification as providing a definition for both "hybridization feature" and "background feature," which, for convenience, is reproduced *infra*, in pertinent part.

[63] A "hybridization feature" is defined as a structure comprised of a plurality of hybridization probes that selectively hybridize to a detectably labeled target nucleotide sequence, wherein the target may be labeled prior to or after hybridization, preferably prior to hybridization, as defined above. In a preferred embodiment, a hybridization feature contains 3.1×10^6 to 6.3×10^7 hybridization probes, preferably 1.6×10^7 to 4.7×10^7, more preferably 2.8×10^7 to 3.5×10^7 hybridization probes.

[64] A "background feature" is defined as a structure comprised of a plurality of background probes that do not selectively hybridize to the target nucleotide sequence, as defined above. A background feature is a feature that provides a signal during a hybridization assay that is made up of three components: (a) a feature substrate background component; (b) a probe background component; and (c) a non-specific binding component. In a preferred embodiment, a background feature is a region of an array that contains background probes covalently bound to the array-surface. In a preferred embodiment, a background feature contains 3.1×10^6 to 6.3×10^7 background probes, preferably 1.6×10^7 to 4.7×10^7, more preferably 2.8×10^7 to 3.5×10^7 background probes.

8. A review of the disclosures fails to find an adequate written description of an adequate number of background probes so as to comply with even the lower limits of the range of background probes required for a background feature (3.1×10^6). Indeed, the specification has been found to contain a Sequence Listing that lists but 53 sequences. Page 15, first paragraph, provides support for "background probes" ranging in length "from about 5 to about 500 nt." As seen in the Sequence Listing, not all of the disclosed sequences fall within the stipulated range.

SEQ ID NO.	LENGTH
1	983
4	1050
19	1034
20	1034
21	1012
22	1204
23	1394
42	1392

However, in accordance with claim 22, a validated background feature is to comprise one of the sequences represented by SEQ ID NO: 1-53. The specification dos not support the position that

nucleic acids represented by SEQ ID NO: 1, 4, 19, 20, 21-23, and 42 could serve as a background probe in a background feature.

Assuming *arguendo*, that the above-identified sequences could be used as a background probe, a position that the Office does not concede, the specification does not provide an adequate written description of any one hybridization feature or of any background feature comprised within said hybridization feature. In view of the claimed method requiring the use of a hybridization feature that comprises a background feature, and the absence of an adequate written description of any one hybridization feature, the specification has not provided an adequate written description of the reagents needed to practice the claimed method. It appears that applicant is attempting to satisfy the written description requirement of 35 USC 112, first paragraph, through obviousness. Obviousness, however, cannot be relied upon for satisfaction of the written description requirement. In support of this position, attention is directed to the decision in *University of California v. Eli Lilly and Co.* (Fed. Cir. 1997) 43 USPQ2d at 1405, citing *Lockwood v. American Airlines Inc.* (Fed. Cir. 1997) 41 USPQ2d at 1966:

> Recently, we held that a description which renders obvious a claimed invention is not sufficient to satisfy the written description requirement of that invention.

9. Additionally, the specification does not reasonably suggest that applicant was in possession of the claimed invention at the time of filing.

10. For the above reasons, and in the absence of convincing evidence to the contrary, claims 13 and 15-23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

11. Claims 15 and 16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 15 and 16 are indefinite as claims 15 and 16 both depend from canceled claim 14.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

14. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

15. Claims 13 and 15-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,723,320 (Dehlinger) in view of US Patent 5,445,934 (Fodor et al.), Blanchard et al. (*Biosensors*, Vol. 11, No. 6/7, pages 687-690, 1996), US Patent 5,563,034 (Brink et al.), and Iitiä et al., BioTechniques, Vol. 17, No. 3, 1994, pages 566-573.

16. Dehlinger, column 13, discloses methods of using arrays of oligonucleotides. Such methods encompass sequencing-by-hybridization, diagnostics, and gene expression. Column 12 specifically teaches that an array may contain internal control sequences. Column l 2 describes an assortment of probes that can range in lengths from 10 to 50 bases in length.

17. Dehlinger does not teach use of applicant's "background nucleic acid feature" nor the use of sequences represented by SEQ ID NOS: 1 to 53 (claim 22).

18. Fodor et al., column 15, discloses the synthesis of arrays of oligonucleotides that comprise up to 10^8 different sequences which, at column 25, are further defined as optionally being dodecanucleotides or larger. The examiner takes notice that an array of 10^8 oligonucleotides would accommodate all possible oligonucleotides 13 bases in length (6.71×10^7 oligonucleotides). Accordingly, an oligonucleotides array comprising all possible l3-mers would, by default, comprise those sequences explicitly recited by applicant that are 13 bases or less in length.

19. Blanchard et al., teach explicitly of the production of oligonucleotide arrays that comprise all possible oligonucleotides of a given length.

20. Neither Fodor et al., nor Blanchard et al., teach the use of sequences that will not hybridize to their complement.

21. Brink et al., columns 3, teaches:

> [I]f there is non-specific probe binding, probe trapping, or insufficient washing, he experimental and negative control probes will respond in the same way. Use of a negative control probe allows one to accurately determine how much of the experimental signal is due to binding of the experimental probe to the target nucleic acid. Without negative controls it is difficult to determine how much of the signal from a hybridization assay is due to background. This can be crucial because in some environmental samples high signal is due entirely or almost entirely to high background. Thus negative controls can be crucial to interpretation of results from hybridization assays.

22. Brink et al., column 3, also teach:

> Running experimental and control hybridizations under different conditions is usually so inconvenient that it is impractical. Even if the experimental and control probes are optimized for the same conditions, if the probes are dissimilar in length, distribution of GC and AT, or any of the other variables that affect hybridization kinetics, the probes will behave differently in hybridization, diminishing the value of the negative control.

23. Brink et al., teaches that these problems an be overcome by using control probes that "are analogous in almost every respect to the experimental probes, except in their ability to bind the intended nucleic acid target."

24. As seen in column 4, the negative control probes are capable of binding to their complement, but not to the target sequence. Brink et al., do not teach of nucleic acid sequences that either do not bind or bind poorly to their complement.

25. Iitiä et al., page 571, center column, teach that they "repeatedly obtained a lower hybridization signal with the probes designed against the sense strand of the target DNA."

26. It would have been obvious to one of ordinary skill in the art at the time the invention was made to performed nucleic acid hybridization assays that contained an internal control

(Fodor et al.) wherein the assay comprised have used as a negative control probe nucleic acid sequences that either do not bind to the target nucleic acid or to the (experimental) probe for a target nucleic acid (Brink et al.) and wherein the assay further comprised performing washing steps prior to detecting a hybridization signal (Brink et al.). It would have also been obvious to said ordinary artisan to have performed said assay where the assay was conducted in association with nucleic acids immobilized in an array format (claim16; Dehlinger, Fodor et al., and Blanchard et al.). As noted by Brink et al., one should select probes that correspond as closely a possible to that of the target nucleic acid. Accordingly, it would have been obvious to said ordinary artisan to have selected probes such as those taught explicitly by Brink et al., a well as other nucleic acid sequences known in the art that exhibit poor or no binding to their complement (Iitiä et al.).

27. For the above reasons, and in the absence of convincing evidence to the contrary, claims 13 and 15-23 are rejected under 35 USC 103(a) as being unpatentable over US Patent 5,723,320 (Dehlinger) in view of US Patent 5,445,934 (Fodor et al.), Blanchard et al. (*Biosensors*, Vol. 11, No. 6/7, pages 687-690, 1996), US Patent 5,563,034 (Brink et al.), and Iitiä et al., BioTechniques, Vol. 17, No. 3, 1994, pages 566-573.

Double Patenting

28. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

29. Claims 13 and 15-23 are provisionally rejected under the judicially created doctrine of double patenting over claims 50-52, 55-60, 62-64, 66-67, 71-73, and 76-84 of copending Application No. 09/398,399. This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

30. The subject matter claimed in the instant application is fully disclosed in the referenced copending application and would be covered by any patent granted on that copending application since the referenced copending application and the instant application are claiming common subject matter, as follows: A hybridization assay that takes into account background signal through the use of background probes.

31. Furthermore, there is no apparent reason why applicant would be prevented from presenting claims corresponding to those of the instant application in the other copending application. See *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968). See also MPEP § 804.

Conclusion

32. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (571) 272-0751. The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

33. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

34. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Bradley L. Sisson
Primary Examiner
Art Unit 1634

BLS
04 May 2004